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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/308,223	08/12/1999	GEORG KALLMEYER	P8341-9011	5876

6449 7590 08/11/2005

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WASHINGTON, DC 20005

EXAMINER

FETTEROLF, BRANDON J

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 08/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No. 09/308,223	Applicant(s) KALLMEYER ET AL.	
	Examiner Brandon J. Fetterolf, PhD	Art Unit 1642	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 07 June 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
 b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
 (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
 (b) ☐ They raise the issue of new matter (see NOTE below);
 (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
 (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
 5. ☐ Applicant's reply has overcome the following rejection(s): _____.
 6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
 7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
 The status of the claim(s) is (or will be) as follows:
 Claim(s) allowed: _____.
 Claim(s) objected to: _____.
 Claim(s) rejected: 13, 15-18, 22-36.
 Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
 9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
 10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____
 12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
 13. ☐ Other: _____.

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Kallmeyer et al.

Response to the Amendment

The Amendment filed on 06/07/2005 in response to the previous Final Office Action (03/08/2005) is acknowledged and has been entered.

Claims 13, 15-18, 22-36 are currently pending and under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Rejections Maintained:

Claims 13, 15-18, 22-36 **remain** rejected under 35 U.S.C. 103(a) as being unpatentable over Andya *et al.* (US Patent No. 6,267,958, March 1996) in view of Michaelis *et al.* (US Patent No. 5,919,443, June 1995) for the reasons of record in the Non-Final Office Action filed on 12/18/2001 (pages 5-6) and the Final Office Action filed on 03/08/2005 (pages 4-5) and for the reasons set forth below.

In reference to the previous action (12/18/2001) which held that it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the lyophilizate of Andya *et al.* so as to include an amino sugar as taught by Michaelis *et al.*, Applicant's submit that the claims, as amended, are directed to stabilizing an antibody lyophilizate with an amino sugar, at least one amino acid, and a surfactant. Applicant's further contend that Andya et al. does not teach or suggest the use of an amino sugar to stabilize a lyophilizate of an antibody. Moreover, Applicant's argue that this failure in Andya *et al.* is not cured by the teachings of Michaelis *et al.*, which is directed to stabilization of lyophilized pharmaceutical preparations of G-CSF. Furthermore, Applicant's assert that although Michaelis *et al.* discloses the use of an amino sugar as a stabilizing agent, the reference is directed to stabilizing C-CSF, a non-glycosylated single polypeptide chain G-CSF, which is very different from the complex antibodies of the currently claimed invention. Thus, Applicants contend that there is no motivation to combine the cited reference to

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teach or suggest the use of an amino sugar in stabilizing an antibody lyophilizate as the amended claims.

These arguments have been carefully considered but are not found persuasive.

First, the Examiner agrees with Applicants submission that the Andya *et al.* reference does not specifically teach or suggest the use of an amino sugar to stabilize a lyophilizate of an antibody. Moreover, the Examiner agrees with Applicants contention that Michaelis *et al.* teach the stabilization of a lyophilized pharmaceutical preparation of G-CSF, which is chemically different from an antibody. However, it must be remembered that the references are relied upon in combination and are not meant to be considered separately as in a vacuum. It is the combination of all of the cited and relied upon references which make up the state of the art with regard to the claimed invention. Furthermore, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference and it is not that the claimed invention must be expressly suggested in any one or all of the references; but rather the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). In the instant case, both references represent analogous teachings comprising the preparation of stable pharmaceutical compositions. Thus, while Applicants contend that there is no motivation to combine the cited references because Michaelis *et al.* teach using an amino sugar for the preparation of lyophilizate of a polypeptide which is chemically different from the presently claimed antibody, the suggestion to combine was based on the advantages of an improved lyophilizate since Michaelis *et al.* makes the surprising discovery that is possible to produce stable forms of pharmaceutical agents when amino sugars are used as additives and further that solid preparations which contain amino sugars as auxiliary agents can be frozen or even stored at increased temperatures with no significant loss of protein quality (12/18/01, page 6). Therefore, Applicant's claimed invention fails to patentably distinguish over the state of the art represented by the cited references taken in combination.

Therefore, NO claim is allowed

All other rejections and/or objections are withdrawn in view of applicant's amendments and arguments there to.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brandon J Fetterolf, PhD
Examiner
Art Unit 1642

BF


JEFFREY SIEW
SUPERVISORY PATENT EXAMINER
4/5/05